Total and partial laparoscopic adrenalectomy

Participants:

Antonio Silvinato²
Wanderley M. Bernardo²
Anibal Wood Branco ¹

Contact: wmbernardo@usp.br

Final version: *January 7, 2018*

1. Brazilian Society of Urology
2. Brazilian Medical Association

INTRODUCTION

The adrenal diseases of interest to urologists are those that require primarily surgical treatment. This group is composed mainly of solid tumors that can originate from various components of the gland, showing a great variety of clinical behaviors depending on their ability to secrete or not adrenal hormones. Macro and micronodular hyperplasias, adrenal gland cysts and pseudocysts, infectious processes such as abscesses and granulomas, and the presence of metastases from tumors of other origins are rarer.

Adrenal gland solid tumors are the primary indication for adrenalectomy and can be classified in various ways: according to the place of origin (cortical tumors, spinal cord tumors and other rarer tumors from the stroma, vessels and nerves), the hormonal profile (functioning tumors and non-functioning tumors), risk of malignancy, among others.

The indication for adrenalectomy is well established in two situations: in functioning tumors and suspicion of malignancy[1]. The hormonal profile of the tumor should always be investigated, regardless of the presence or absence of clinical manifestations and the size of the tumor. Recent studies have demonstrated that approximately 20% of patients with adrenal incidentaloma have some form of subclinical hormonal imbalance and may represent a population at greater risk of metabolic and cardiovascular disorders[1]. This assessment is particularly important in cases that will be submitted to surgical treatment since it brings clinical and anesthetic implications, especially related to systemic arterial pressure and hydroelectrolytic balance.

There is a consensus that all functioning cortical or medullary tumors must be surgically removed. With respect to non-functioning tumors, a biopsy does not bring any benefits, except in rare situations of bilateral tumors and suspected systemic or secondary disease.

The suspicion of malignancy is linked to tomo-

graphic findings. There is a direct correlation between the size of the tumor and the potential for malignancy. The adrenocortical carcinomas represent 2% of the tumors smaller than 4 cm, 6% of the tumors between 4.1 and 6 cm and 25% of the tumors larger than 6 cm[2]. Thus, lesions smaller than 3 cm are usually benign adenomas and are not necessarily removed but can be monitored. Tumors larger than 6 cm are normatively operated; those of intermediate size (3 to 6 cm) must be considered individually, and the presence of other signs of malignancy (heterogeneity, calcifications, rapid growth, low body fat percentage, among others) must be observed and can be further investigated radiologically (magnetic resonance imaging) and monitored serially[2]. Therefore, the adrenocortical carcinomas are generally large (>6 cm) and exhibit a heterogeneous radiological pattern and a great tendency of involvement of adjacent structures. Since these are potentially aggressive tumors, adrenocortical carcinomas should be treated radically, with en bloc resection of the tumor and adjacent structures affected associated with regional lymphadenectomy[3].

Laparoscopy has been considered, for some time, the preferential treatment for benign diseases of the adrenal glands. As the benefits of the laparoscopic access were demonstrated and the technical improvement was consolidated, indications for this route of access expanded and absolute contraindications reduced[3,4].

TECHNICAL ASPECTS
Preoperative preparation

Patient preparation for the surgical procedure is vital and must be multidisciplinary, involving, whenever possible, the urologist, endocrinologist, and anesthesiologist. Functioning tumors require additional care, relating, in particular, to the effect of hormonal overload-deprivation. Knowledge of the physiopathology of adrenal glands, as well as the effects of hormonal overload, is indispensable.

Basic principles for adrenal surgeries
- Appropriate and individualized preparation.
- Minimal manipulation of the gland to prevent rupture and tumor implant.
- Early ligation of the adrenal vein, when possible, which must precede the manipulation of the gland.

Operative technique

The technique of laparoscopic adrenalectomy has been widely described[5,6]. Briefly, the primary steps of the technique are listed below.

Immediate preoperative cares
- Antimicrobial chemoprophylaxis during anesthetic induction.
- Orogastric or nasogastric intubation, to be removed immediately upon completion of the procedure. Dispensable in procedures performed using retroperitoneoscopy.
- Urinary catheterization delay.

Patient positioning
- Transperitoneal procedure.
- Lateral decubitus at 45 to 60 degrees opposite to the gland that will be operated, ipsilateral upper limb elevated and attached to the arc of the operating table and the contralateral next to the body. The surgical team is positioned facing the patient's abdomen.

Retroperitoneal procedure
- Total lateral decubitus. The surgical team is positioned facing the patient's back.
- Pads should be placed to protect surfaces from friction, and the patient must be positioned on the table with adhesive tape.

ACCESS TO THE WORK AREA
Transperitoneal

The iliac crest, the costal margin, and umbilical scar are used as reference points for the introduction of the trocars.

Usually, four 10/11 mm trocars are used (umbilical scar, the middle line below the xiphoid appendix junction, costal margin, and point between the umbilical scar and the anterior superior iliac spine). In slim patients and children, two 10/11 mm and two 5 mm trocars are used.

A puncture is performed using a Veress needle in the median line, at the edge of the umbilical scar or the midclavicular line on the side that will be operated. The initial access must always be secure, so in special situations, the Veress needle should be replaced by a Hasson cannula or a balloon trocar inserted by minilaparotomy.

Retroperitoneal

The iliac crest, the 12th rib, and the paravertebral muscles are used as points of reference. The trocars can be introduced by direct vision or guided by the index finger, once you have created the surgical space.

Incision of approximately 2 cm below and immediately preceding the 12th rib (inferior lumbar Petit's triangle), followed by perforation of the lumbodorsal fascia, introduction of the index finger into the retroperitoneal region to create space by finger dissection. At this stage, the psoas muscle and the lower pole of the kidney must be digitally recognized. The use of a Gaur balloon is optional.

Insufflation

From the initial phase of the procedure until the trocars are completely introduced, the intracavitary pressure can be maintained between 15 and 18 mmHg. After the access is completely obtained, the pressure can be reduced to 12 mmHg.

STEP BY STEP PROCEDURE
Transperitoneal

Medial release of the colon - exposure of the anterior renal fascia and the large vessels. In proceedings on the right side, the colon usually does not need to be mobilized. Whereas on the left side, a broad mobilization of the colon from the splenic flexure up to the sigmoid is always necessary. For the medial mobilization of the spleen and the tail of the pancreas, which is not always indicated, it is necessary to make an incision on the parietal peritoneum cranially to the left subphrenic space, up to the diaphragm. This extensive mobilization allows gravity to move the left colon and the tail of the pancreas medially.

Dissection of the medial face of the gland — on the right side, the dissection should be performed next to the inferior vena cava, through the incision of the peritoneal reflection on the right edge of the vein. Then, the right adrenal vein, tributary of the inferior vena cava, is dissected with sections between metal or polymer clamps. This initial medial dissection favors the identification of the adrenal vein and its junction with the inferior vena cava when the gland receives lateral traction.

On the left side, the inferomedial portion of the gland is the starting point. The left renal vein is identified, more specifically its upper edge, where the left adrenal vein is identified and sectioned between clamps. The left adrenal gland is in close contact with the vessels of the renal pedicle, which requires greater attention during the inferomedial dissection.

Retroperitoneal

After the medial dissection and ligation of the adrenal vein, an incision is made on the renal fascia, and the gland is separated from the surface of contact with the upper pole of the kidney. Finally, the superior and lateral edges are separated from adjacent structures by means of delicate dissection, cauterization, and section of small arterial, venous and lymphatic vessels.

Removal of the specimen

Is done with the aid of an extraction sac. The entire piece is removed and should not be morcellated.

Partial adrenalectomy

Partial adrenalectomy requires the following technical steps, in addition to those already described:

Dissection of the gland, preferably without the ligation of the adrenal vein; section of the region compromised, with a margin of safety, by means of a 35 mm linear vascular stapler and incision with an ultrasonic scalpel or polymer clamps; review of hemostasis in recalcitrant part of the gland.

METHOD

We evaluated the therapeutic role of laparoscopic adrenalectomy based on a systematic review of the literature with no time restriction on the Medline database using the following descriptors: (Adrenalectomy OR adrenalectom*) AND (Laparoscopy OR laparoscop* OR endoscop* OR Robotic Surgical Procedures OR robotic*) AND (Random* OR Comparative study OR Comparative studies OR systematic[sb]). Were retrieved 473 papers, and of these, 16 were selected to answer the clinical question: Is laparoscopic adrenalectomy effective and safe in the treatment of surgical diseases of the adrenal gland?

The "Measurement Tool to Assess Reviews" (Amstar)27 was used to evaluate the quality of the systematic reviews. This tool provides a global quality rating on a scale from 0 to 11, in which 11 represents a review of the highest quality. Quality categories were determined as follows: low (0 to 3 score), medium (4 to 7 score) and high (8 to 11 score). SRs of low and medium quality were excluded.

The recommendations presented by the authors of the review had their strength estimated according to the Oxford/Grid.

RESULTS

Oncologic effectiveness of the laparoscopic access

To this moment, there have been no randomized controlled clinical trials (RCT) to guide or support the use of laparoscopic resection in adrenocortical carcinoma or malignant pheochromocytoma.

Adrenal carcinomas are rare tumors, with an incidence of 1-2 new cases per million people every year, representing 0.05% to 0.2% of malignant neoplasms. Most adrenal tumors are sporadic; however, some genetic syndromes increase the risk of adrenal tumorigenesis. The treatment of adrenal carcinoma includes resection of the primary tumor, resection of metastases and systemic chemotherapy. In the presence of disseminated disease, the answer to any form of treatment is very bad.

Walz et al. reported a prospective series of 560 retroperitoneal adrenalectomies, including tumors of up to 10 cm. Although technically challenging, it is possible to remove tumors of 6-7 cm via laparoscopic access; however, tumors larger than 6 cm are most often malignant[7,8](B).

A systematic review (SR) with meta-analysis, including nine historical cohort studies, compared laparoscopic and open adrenalectomy in 797 patients with adrenocortical carcinoma. Tumors treated with laparoscopy were smaller (p<0.001) and exhibited a greater proportion in the stadium (I or II) (p<0.001), in relation to tumors treated with open adrenalectomy. Laparoscopic adrenalectomy was associated with a shorter hospitalization time (mean difference (MD] -2.51 days, 95% CI -3.31 to -1.72, p<0.001) in the analysis of four studies with 266 patients; increased peritoneal carcinomatosis in recurrence (risk ratio [RR] 2.39, CI 95%: 1.41-4.04, p=0.001) in the analysis of five studies with 408 patients; non-significant decrease in mortality due to cancer (risk ratio [RR] 8%, 95% CI -17% to 1%) in the analysis of six studies with 499 patients. There was no difference between the two groups for postoperative complications in the analysis of four studies with 266 patients and the rate of recurrence in the analysis of nine studies with 797 patients; the results were limited by high heterogeneity[9](A).

Therefore, laparoscopic adrenalectomy is not the preferred approach for masses that are primary adrenal cancer[9](A).

Laparoscopic surgery in relation to perioperative parameters

A historical cohort study included 80 patients (mean age of 48 years) undergoing lateral transperitoneal laparoscopic adrenalectomy (n=40) or lateral transperitoneal open adrenalectomy(n=40) for removal of functional adenomas and adrenal masses <6 cm, with a mean follow-up time of 30 months. The patients in each group were compared regarding age, endocrine disorder, body surface area, side and size of the tumor. Aldosterone-producing adenomas were present in 41% of the cortisol-producing adenomas in 16%, pheochromocytomas in 19%, and non-functioning adenomas in 24%. Laparoscopic surgery, compared with the open approach: increased the average time of surgery (147 *vs.* 79 minutes; p<0.05) and reduced the use of analgesics in the postoperative period (average of doses = 2.9 *vs.* 5.2; p<0.05), the length of hospital stay (12 *vs.* 18 days; p<0.05), as well as the rate of late complications (pain, dysesthesia, muscle weakness = 0% *vs.* 47.5%, p < 0.05). There was no difference in time for oral ingestion, time for ambulation, and intraoperative or early complications. We conclude that the laparoscopic access presents superior results for peri- and postoperative parameters, such as a reduction in the use of analgesics, shorter time of hospital stay and late morbidity, when compared with the open access[10](A).

The choice between trans and retroperitoneal access for surgical procedures of the adrenal gland

A SR with meta-analysis of two small randomized clinical trials (RCTS) and 20 observational studies compared the retroperitoneoscopic and laparoscopic adrenalectomy in 1,966 adult patients with non-malignant adrenal tumors. A total of 709 patients underwent retroperitoneoscopic adrenalectomy (lateral or posterior), and 1,257 had laparoscopic adrenalectomy. Retroperitoneoscopic surgery was associated with a reduction in hospital stay time in the analysis of 14 studies and a total of 829 patients; however, this result is limited by high heterogeneity. There was no difference between the two procedures for the outcomes of mortality, hemorrhage, the overall risk of complications, conversion to open adrenalectomy, time for oral ingestion and time to ambulation[11](A).

Two studies, one RCT and a historical cohort, published retrospectively and not included in this SR, also compared access routes.

In the RCT, 65 adult patients with benign adrenal tumors ≤7 cm were randomized to posterior retroperitoneoscopic adrenalectomy or lateral transperitoneal adrenalectomy and followed-up for five years. The posterior retroperitoneoscopic adrenalectomy improved perioperative outcomes (intraoperative blood loss, pain during 48 postoperative hours, less time for oral ingestion, ambulation and hospital stay [p<0.001 for each], reduction of nausea [p=0.029]), in comparison with the lateral transperitoneal laparoscopic adrenalectomy. Posterior retroperitoneoscopic adrenalectomy reduced surgical time (50.8 minutes *vs.* 77.3 minutes; p<0.001) and the risk of incisional hernia (0% *vs.* 16.1%, p=0.022), NNH 6 for lateral approach, there were no surgical conversions[12](A).

In a retrospective cohort study, 251 patients (mean age 52 years) had 279 retroperitoneal laparoscopic adrenalectomies with the retrograde (n=107) or anterograde approach (n=172). A total of 38% had Cushing's syndrome, 27% Conn syndrome, 16% pheochromocytoma, and 11% non-functioning adenoma. The retrograde approach, in comparison with the anterograde, reduced: surgical time (101 minutes *vs.* 140 minutes; p<0.001), postoperative consumption of morphine (9.4 mg *vs.* 15.7 mg; p=0.026) and permanence in the intermediate unit (1.3 days *vs.* 1.8 days, p= 0.001). There was no difference in the rates of pre- or postoperative complications, as well as in mortality between the two groups[13](A).

Therefore, the choice between the trans and retroperitoneal approaches must be individualized and depends on specific situations related to the patient (obesity, previous surgery on the upper floor of the abdomen, among others), and the preference of the surgeon.

Indication for partial adrenalectomy

A "before and after" study included 93 patients (mean age of 38 years) with benign unilateral adenoma and hypercortisolism who had partial adrenalectomy and were followed-up for ≥1 year. The surgery was performed via retroperitoneal laparoscopic approach in 60 patients (65%), and the other 33 (35%) underwent open surgery. Six patients underwent conversion to total adrenalectomy due to recurrent disease or tumor size ≥5cm. All patients received

therapy with postoperative cortisone for an average of 6.2 months. Surgery was associated with the resolution of hypercortisolism in 98% of patients (91 out of 93), hypertension in 53% (34 out of 64), diabetes in 26% (7 out of 27), obesity (body mass index ≥ 30 kg/m²) in 58% (28 out of 48). Partial adrenalectomy via retroperitoneal laparoscopic approach, compared with the open adrenalectomy, demonstrated: (average) time of surgery (80 minutes *vs.* 125 minutes; p<0.01), intraoperative complications (1.7% *vs.* 9.1%; p=not reported) and length of hospital stay (7 days *vs.* 11 days - mean - p<0.01)[14](B).

One RCT compared partial adrenalectomy (n=104) *versus* total adrenalectomy (n=108), via retroperitoneal laparoscopic approach, in 212 patients with unilateral aldosterone-producing adenomas (2 cm on average); those with previous adrenal surgery on the same side were excluded. Both techniques were similar in the functional and perioperative parameters (surgical time, length of hospital stay, improvement of hypertension in up to eight years [NNT = not significant])[15](A).

It is concluded that the partial laparoscopic retroperitoneal adrenalectomy is effective and safe in patients with unilateral benign adenoma and hypercortisolism.

Adrenalectomy for patients with subclinical Cushing's syndrome

A significant portion of adrenal adenomas produce small amounts of cortisol autonomously, which are insufficient to cause the classical stigmata of Cushing's syndrome, but sufficient to determine subtle alterations in the hypothalamic-pituitary-adrenal axis. This clinical condition is known as subclinical Cushing's syndrome.

In a small RCT, without direct comparisons, 45 patients (mean age of 64 years) with subclinical Cushing's syndrome (SCS) and adrenal incidentaloma (3.5 cm on average) were randomized to receive lateral transperitoneal laparoscopic adrenalectomy or the conservative approach and were followed-up, on average, for 7.7 years. In the surgical group, diabetes mellitus normalized or improved in 62.5% of patients (5 out of 8), hypertension in 67% (12 out of 18), hyperlipidemia in 37.5% (3 out of 8), and obesity in 50% (3 out of 6). No change in bone parameters was observed after surgery in SCS patients with osteoporosis. On the other hand, some complications of DM, hypertension, and hyperlipidemia were ob-

served in patients who underwent the conservative treatment[16](B).

Laparoscopic adrenalectomy in pheochromocytoma

Most of the times, pheochromocytoma is a non-familial sporadic tumor. However, it can present itself as a genetic disease, with an autosomal dominant inheritance of high penetrance, occurring in isolation or associated with other pathologies.

In patients with pheochromocytoma, laparoscopic adrenalectomy can be as secure as open adrenalectomy, reducing the length of hospital stay, in an analysis including a small RCT and two retrospective cohort studies.

In the RCT, 22 patients with sporadic pheochromocytoma (non-familial) were randomized for laparoscopic vs. open adrenalectomy. The length of hospital stay, on average, was five days in the laparoscopic group vs. eight in the open approach group (p<0.05). There was no difference in the number of patients with hypertensive peaks during the intraoperative period or on the number of hypertensive peaks per patient[17](B).

In the first retrospective cohort, 44 patients underwent surgery for pheochromocytoma. The perioperative results of 30 laparoscopic surgeries (LA) were compared with 14 open surgeries (OA). The laparoscopic adrenalectomy group presented a smaller size of tumor (3.9 cm vs. 5 cm, p<0.05), the laparoscopic surgery reduced the length of hospital stay (median of 3 days for LA vs. 6 days for OA; p<0.05), there was no difference between the groups for the outcomes of surgery time, rate of postoperative complications, intraoperative hypertensive episodes, intraoperative complications related to hypertensive peaks, and risk of recurrence (duration of follow-up not reported)[18](B).

The second retrospective cohort compared to laparoscopic adrenalectomy for pheochromocytoma in seven patients vs. open resection in nine patients. Laparoscopic adrenalectomy compared with the open approach reduced: episodes of hypertension per procedure 1 vs. 2 (p=0.008), number of patients who needed vasoconstrictor drugs 2 vs. 8 (p=0.035), length of hospital stay (median 3 days vs. 6 days; p= 0.001), and number of patients who needed postoperative opioid 1 vs. 9 (p=0.001). There was no difference in perioperative complications between both groups[19](B).

Laparoscopic adrenalectomy is an option in the treatment of pheochromocytoma in the sporadic form (non-familial).

Robotic adrenalectomy

A systematic review of nine studies (a small randomized study and eight observational studies) compared robotic and laparoscopic adrenalectomy in 600 patients with adrenal masses. Robotic adrenalectomy compared with laparoscopic reduced: length of hospital stay (mean difference in days [MD] = -0.43 95% CI -0.56 to -0.3, I^2 = 88%), bleeding (MD = -18.21 ml, CI 95% -29.11 ml to -7.32 mL; I^2 = 90%). There was no difference in the rate of complications (ARR = -0.04; 95% CI = -0.07 to 0.0; p=0.05; I^2=0%), as well as the conversion rate (odds ratio [OR] = 0.82; 95% CI = 0.39 to 1.75; I^2=0%) or time of surgery (MD = 5.88 min.; 95% CI = -6.02 to 17.79; I^2=96%)[20](A).

A SR with recent meta-analysis included 13 studies that compared robotic and laparoscopic adrenalectomy. Robotic adrenalectomy was associated with a longer surgical time (OR = +15,60, IC95% +2.12 the +29.08; I^2=77.4%), but a shorter length of hospital stay (OR = -0.40, 95% CI = -0.64 to -0.17; I^2=78.3%). There was no difference in terms of intraoperative and postoperative complications, mortality and conversion rates[21](A).

The high heterogeneity (I^2) should be considered in the analysis of the results of both meta-analyses.

Robotic adrenalectomy is a therapeutic option; however, studies show results with minimal clinical significance.

Laparoendoscopic single site (Less)

A systematic review with meta-analysis including retrospective studies, with a total of 443 patients, compared to Less-AD and conventional laparoscopic adrenalectomy (171 patients in the Less group and 272 in the adrenalectomy group, in a total of nine studies). There was no significant difference in the estimated loss of blood, time for resuming oral intake and length of hospital stay between the two groups. Less-AD patients had a postoperative pain score based on the visual analogue scale significantly lower in comparison with the LC-AD group, but with a longer operative time. Both groups had comparable scores of cosmetic satisfaction. The two groups had a comparable rate of complication, conversion, and transfusion[22](C).

Less-AD can be considered an alternative to con-

ventional laparoscopic adrenalectomy but requires further studies[22](C).

Laparoscopic adrenalectomy in patients with previous abdominal surgery

A retrospective cohort study including 246 patients with laparoscopic adrenalectomy showed that there was no difference in the time of surgery, intraoperative blood loss, and the rate of perioperative complications in patients with previous abdominal surgery, compared with patients with no previous abdominal surgery[23](A).

RECOMMENDATION

- Laparoscopic adrenalectomy is not the preferred approach for masses that are primary adrenal cancer. (A)
- Laparoscopic access presents superior results for peri- and postoperative parameters, with a reduction in the use of analgesics, shorter time of hospital stay and late morbidity, when compared with open access. (A)
- The choice between the trans and retroperitoneal approaches must be individualized and depends on specific situations related to the patient (obesity, previous surgery on the upper floor of the abdomen, among others), and the preference of the surgeon. (A)
- Partial laparoscopic retroperitoneal adrenalectomy is effective and safe in patients with unilateral benign adenoma and hypercortisolism. (A)
- There are benefits in the surgical treatment (laparoscopic) for reducing the risk of metabolic syndrome (glucose intolerance), hypertension and dyslipidemia in patients with subclinical Cushing's syndrome. (B)
- Laparoscopic adrenalectomy is an option in the treatment of pheochromocytoma in the sporadic form (non-familial). (B)
- Robotic adrenalectomy is a therapeutic option; however, studies show results with minimal clinical significance. (A)
- Less-AD can be considered an alternative to conventional laparoscopic adrenalectomy but requires further studies. (C)
- Prior abdominal surgery is not a contraindication for laparoscopic adrenalectomy. (A)

REFERENCES

1. NIH state-of-the-science statement on management of the clinically inapparent adrenal mass ("incidentaloma"). NIH Consens State Sci Statements 2002;19:1-25.

2. Gill IS SD, Nelson D. Laparoscopic versus open adrenalectomy in 210 patients: Cleveland Clinic experience with 210 cases.. In: J Urol Suppl 1999.

3. Gagner M, Lacroix A, Bolte E. Laparoscopic adrenalectomy in Cushing's syndrome and pheochromocytoma. N Engl J Med 1992;327:1033.

4. Gagner M, Pomp A, Heniford BT, Pharand D, Lacroix A. Laparoscopic adrenalectomy: lessons learned from 100 consecutive procedures. Ann Surg 1997;226:238-46; discussion 46-7.

5. LN C. Adrenalectomia laparoscópica – 10 anos de experiência. In: Arq Bras Endocrinol Metab. São Paulo; 2004.

6. Castilho LN, Mitre AI, Arap S. Laparoscopic adrenal surgery in a Brazilian center. J Endourol 2003;17:11-8.

7. Walz MK, Alesina PF, Wenger FA, Deligiannis A, Szuczik E, Petersenn S, et al. Posterior retroperitoneoscopic adrenalectomy--results of 560 procedures in 520 patients. Surgery 2006;140:943-8. PMID:17188142

8. Toniato A, Boschin IM, Opocher G, Guolo A, Pelizzo M, Mantero F. Is the laparoscopic adrenalectomy for pheochromocytoma the best treatment? Surgery 2007;141:723-7. PMID: 17560248

9. Autorino R, Bove P, De Sio M, Miano R, Micali S, Cindolo L, et l. Open Versus Laparoscopic Adrenalectomy for Adrenocortical Carcinoma: A Meta-analysis of Surgical and Oncological Outcomes. Ann Surg Oncol 2016;23:1195-202. PMID: 26480850

10. Imai T, Kikumori T, Ohiwa M, Mase T, Funahashi H. A case-controlled study of laparoscopic compared with open lateral adrenalectomy. Am J Surg 1999;178:50-3; discussion 54. PMID: 10456703

11. Constantinides VA, Christakis I, Touska P, Palazzo FF. Systematic review and meta-analysis of retroperitoneoscopic versus laparoscopic adrenalectomy. Br J Surg 2012;99:1639-48. PMID: 23023976

12. Barczyński M, Konturek A, Nowak W. Randomized clinical trial of posterior retroperitoneoscopic adrenalectomy versus lateral transperitoneal laparoscopic adrenalectomy with a 5-year follow-up. Ann Surg 2014;260:740-7; discussion 747-8. PMID: 25243546

13. Huyghe E, Crenn G, Duly-Bouhanick B, Vezzosi D, Bennet A, Atallah F, et al. Retroperitoneoscopic adrenalectomy: comparison of retrograde and antegrade approach among a series of 279 cases. Urology 2013;81:85-91. doi PMID: 23273074

14. He HC, Dai J, Shen ZJ, Zhu Y, Sun FK, Shao Y, et al. Retroperitoneal adrenal-sparing surgery for the treatment of Cushing's syndrome caused by adrenocortical adenoma: 8-year experience with 87 patients. World J Surg 2012 May;36(5):1182-8. PMID: 22382766

15. Fu B, Zhang X, Wang GX, Lang B, Ma X, Li HZ, et al. Long-term results of a prospective, randomized trial comparing retroperitoneoscopic partial versus total adrenalectomy for aldosterone producing adenoma. J Urol 2011;185:1578-82. PMID: 21419437

16. Toniato A, Merante-Boschin I, Opocher G, Pelizzo MR, Schiavi F, Ballotta E. Surgical versus conservative management for subclinical Cushing syndrome in adrenal incidentalomas: a prospective randomized study. Ann Surg. 2009;249:388-91. PMID: 19247023

17. Tiberio GA, Baiocchi GL, Arru L, Agabiti Rosei C, De Ponti S, Matheis A, et al. Prospective randomized comparison of laparoscopic versus open adrenalectomy for sporadic pheochromocytoma. Surg Endosc 2008; 22:1435-9. PMID: 18398641

18. Humphrey R, Gray D, Pautler S, Davies W. Laparoscopic compared with open adrenalectomy for resection of pheochromocytoma: a review of 47 cases. Can J Surg 2008;51:276-80. PMID: 18815650

19. Edwin B, Kazaryan AM, Mala T, Pfeffer PF, Tønnessen TI, Fosse E. Laparoscopic and open surgery for pheochromocytoma. BMC Surg 2001;1:2. PMID: 11580870

20. Brandao LF, Autorino R, Laydner H, Haber GP, Ouzaid I, De Sio M, et al. Robotic versus laparoscopic adrenalectomy: a systematic review and meta-analysis. Eur Urol 2014;65(6):1154-61. PMID: 24079955

21. Economopoulos KP, Mylonas KS, Stamou AA, Theocharidis V, Sergentanis TN, Psaltopoulou T, et al. Laparoscopic versus robotic adrenalectomy: A comprehensive meta-analysis. Int J Surg 2017;38:95-104. PMID: 28043926

22. Wang L, Wu Z, Li M et al. Laparoendoscopic single-site adrenalectomy versus conventional laparoscopic surgery: a systematic review and meta-analysis of observational studies. J Endourol 2013; 27: 743–50

23. Morris L, Ituarte P, Zarnegar R, Duh QY, Ahmed L, Lee J, et al. Laparoscopic adrenalectomy after prior abdominal surgery. World J Surg. 2008;32(5):897 903. PMID: 18228091

24. Levels of Evidence and Grades of Recommendations - Oxford Centre for Evidence Based Medicine. Disponível em http://www.cebm.net/ blog/2009/06/11/oxford-centre-evidence-based medicine-levels-evidence-march-2009/

25. Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials 1996; 17:1-12

26. Wells G, Shea B, O'Connell D, Robertson J, Peterson J, Welch V, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality ofnonrandomizedd studies in meta-analyses. Disponível em: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.

27. Shea BJ, Hamel C, Wells GA, Bouter LM, Kristjansson E, Grimshaw J et al. AMSTAR is a reliable and valid measurement tool to assess the methodological quality of systematic reviews. J Clin Epidemiol 2009; 62:1013-20. PMID: 19230606 (http://amstar.ca/Amstar_Checklist.php)

28. Guyatt G, Gutterman D, Baumann MH, Addrizzo-Harris D, Hylek EM, Phillips B et al. Grading strength of recommendations and quality of evidence in clinical guidelines: report from an american college of chest physicians task force. Chest 2006;129(1):174-81. PMID: 16424429